



Hypertension and Renal Disease

Sewell I. Kahn, MD FACP

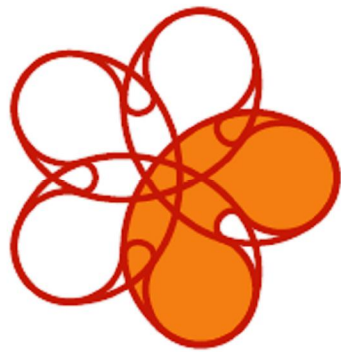
**10th Annual Diabetes/Heart Disease &
Stroke Prevention Winter Symposium**

March 10.2012



Hypertension and Renal Disease

This Presentation is Supported by



**National Kidney
Foundation®**





Objectives (1)

- Review relationships between hypertension and renal disease
- Review pathophysiology of hypertension and relate it to renal disease and the choice of antihypertensives
- Current guidelines



Objectives (2)

- Examine newer guidelines from UK to project what changes we may see in future
- Review an interesting study from Spain that may effect guidelines in the future



Hypertension Classification

- Primary or essential hypertension
- Secondary:
 - é Renal (acute & chronic)
 - Renal disease primary and secondary
 - Renal vascular
 - é Adrenal
 - Primary aldosteronism
 - Cushing's disease
 - Pheochromocytoma
 - Other
- Secondary (continued)
 - é Other endocrine
 - é Hyperthyroidism
 - é Hypothyroidism
 - é Hyperparathyroidism
 - é Sleep apnea
 - é Coarctation of the aorta
 - é Drugs
 - é Other



High Blood Pressure End Organ Effects

- Heart:

LVH *, Angina & MI , CHF

* Increased heart failure, ventricular arrhythmia, fatal MI, and sudden death

- Kidney:

Chronic Kidney Disease

Malignant Nephrosclerosis

- Brain:

Strokes (Both ischemic and hemorrhagic)

- Peripheral Blood Vessels:

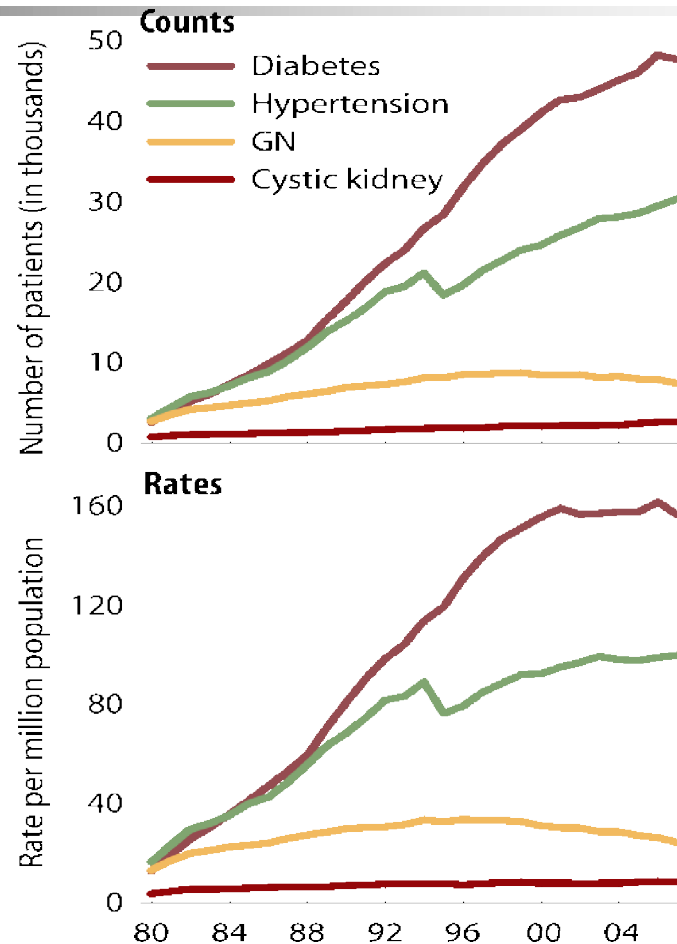
Aneurysm, Claudication

Incident Counts & Adjusted rates, by Primary Diagnosis

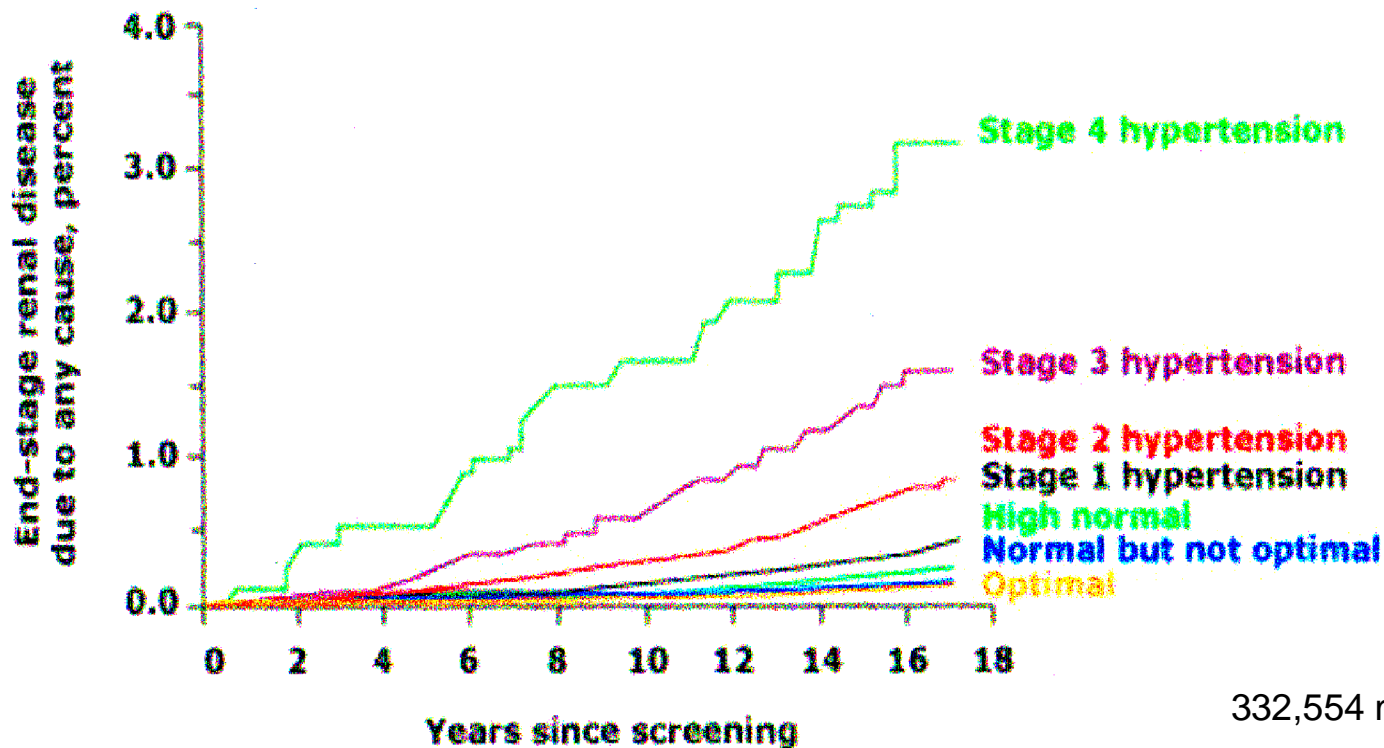
**Diabetes
and Hypertension
are the
Major Causes of CKD**

Prevalence 3rd Qtr 2009
Diabetes 213,421 (37.4%)
High BP 139,616 (24.5%)
Total 570,130

Usrd.org (Accessed 8/28/10)



Relation between hypertension and development of ESRD



MRFIT Study NEJM 1996;334:13 (redrawn by UpToDate©)



Hypertension and Kidney Disease

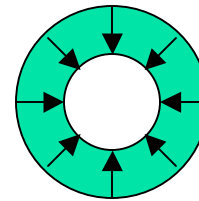
A reciprocal relationship



Blood Pressure Control

$$BP = CO \times PR$$

CO:
Stroke Volume
Heart Rate

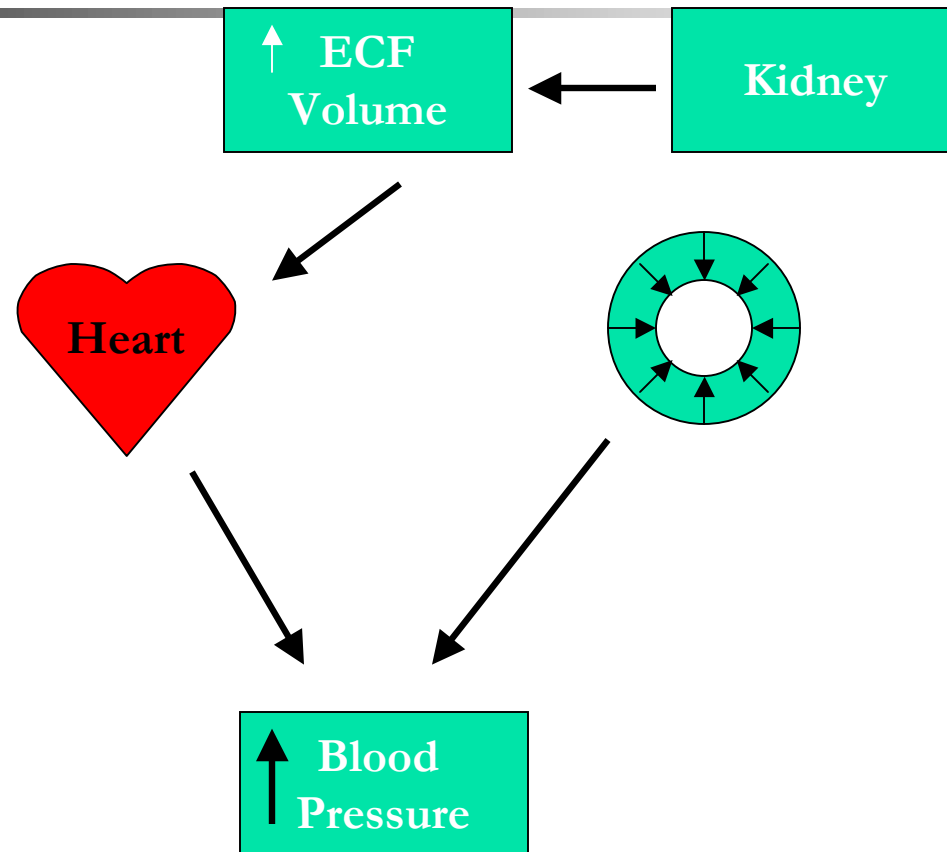


PR:
Vessel Function
Vessel Structure

Blood
Pressure

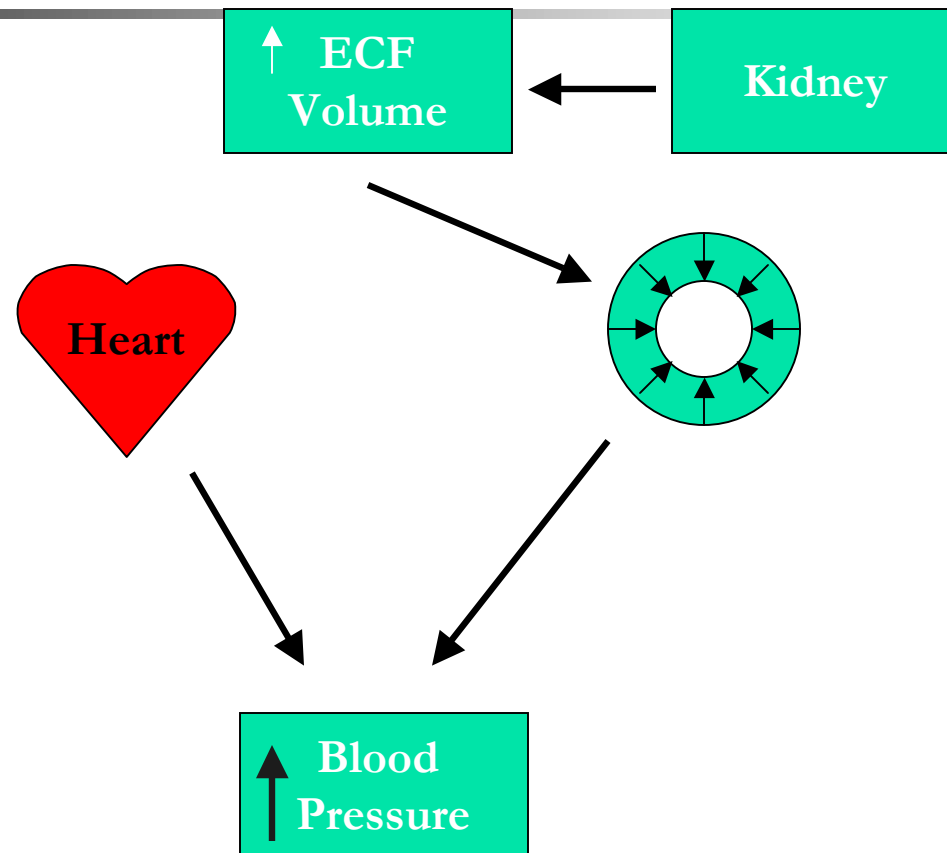
Blood Pressure Control

Effect of Volume overload

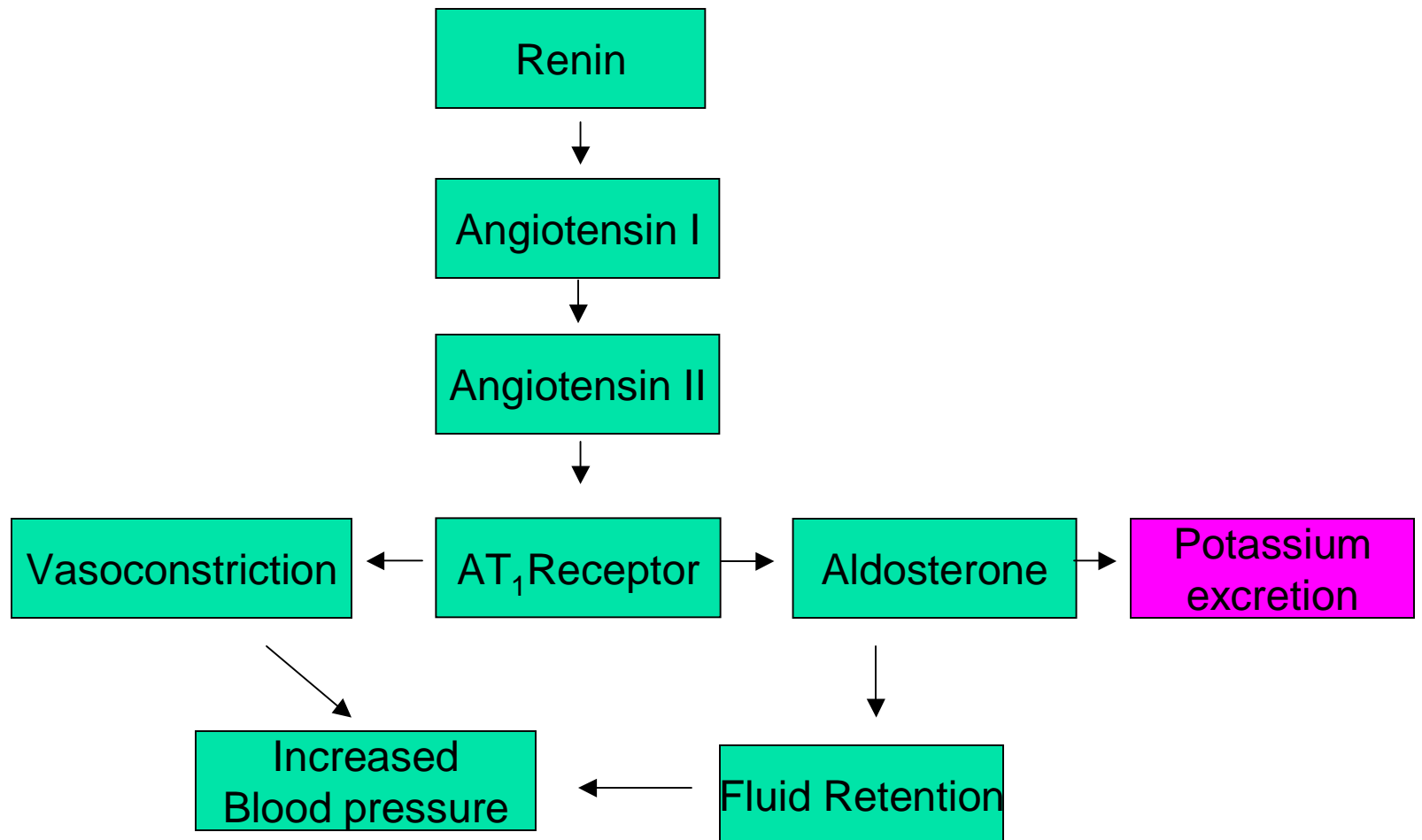


Blood Pressure Control

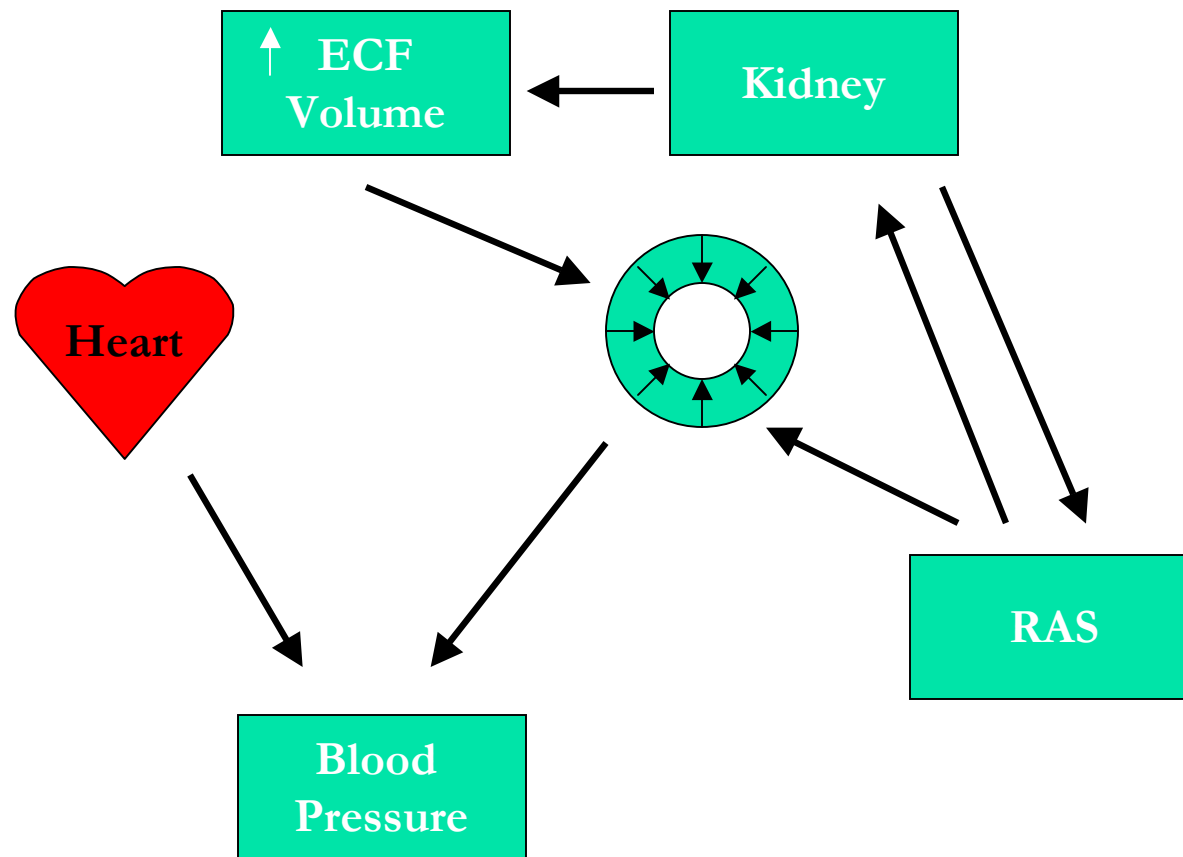
Effect of Volume overload



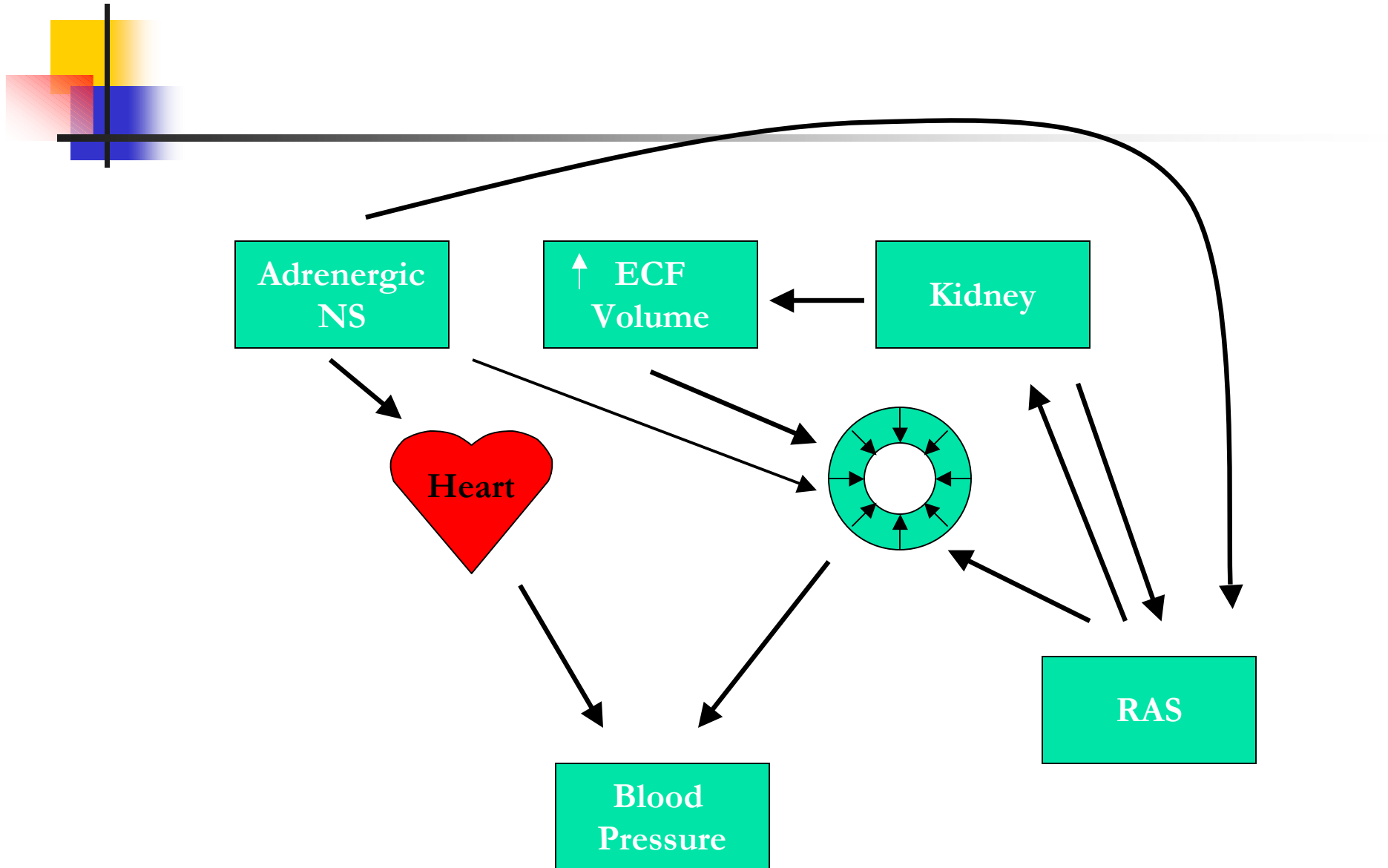
Renin Angiotensin System

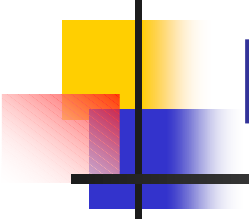


Blood Pressure Control Renal



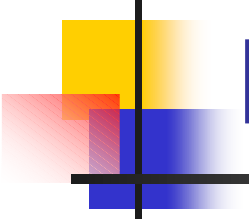
Blood Pressure Control





Renal Disease and Hypertension(1)

- Glomerular Disease
 - Volume expansion
 - Primary treatment: Diuretics
- Renal Vascular Disease
 - Elevation RAS
 - Primary treatment: ACEI/ARB
 - Exception: Volume Expansion(Bilateral Renal Artery Stenosis or RVD in a solitary kidney)



Renal Disease and Hypertension(2)

- Chronic Kidney Disease
 - Volume expansion
 - Elevation RAS
 - Secondary Hyperparathyroidism
 - Other



Drugs and High Blood Pressure

- Oral Contraceptives
- Anabolic Steroids
- Cortisone
- Antidepressants (tricyclic and others)
- Pain/Arthritis Drugs (NSAIDs)
- Lithium
- Transplant Medications
- Nasal Decongestants
- Amphetamines
- Cocaine
- Erythropoietin
- Others



Definition of CKD

“ **Kidney damage for ≥ 3 months**

- . Defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR)

“ **GFR < 60 mL/min/1.73 m² for ≥ 3 months**

“ **New staging for CKD is primarily based on kidney function**

National Kidney Foundation (NKF). *Am J Kidney Dis.* 2002;39(2 suppl 1):S1-S266.



Stages and Prevalence Chronic Kidney Disease

Stages	eGFR (ml/min/1.73m ²)	Prevalence
Stage 5	< 15	526,343
Stage 4	15-29	700,000
Stage 3	30-59	15,500,00
Stage 2*	60 -89	6,500.00
Stage 1*	> 90	3,600,000

USRD Annual
Report 2009

Coresh J et al.
JAMA 2007;298
(17):2028-2047

*** With structural or functional abnormalities**



Stages and Prevalence Chronic Kidney Disease

Stages	eGFR (ml/min/1.73m ²)
Stage 5	< 15
Stage 4	15-29
Stage 3b	30-44
Stage 3a	45-59
Stage 2*	60 -89
Stage 1*	> 90

Use suffix (P)
to denote
presence of
proteinuria

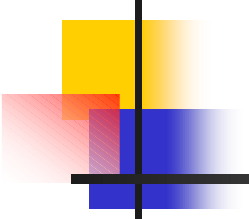
NICE CKD 73
2008

*** With structural or functional abnormalities**

ESRD Rate

adjusted rate per/1000 person-years

Effect of Proteinuria



E GFR ml/min/1.73 m ²	Normal <30 mg/g	Mild(1+) 30-300 mg/g	Heavy(2+) > 300 mg/g
≥ 60	0.03 (62/754158)	0.05 (11/58400)	1.0 (35/8013)
45-59.9 (Stage 3a)	0.2 (27/68768)	0.7 (19/8783)	4.3 (39/2294)
30-44.9 (Stage 3b)	1.3 (36/11823)	4.2 (40/3296)	16.1 (103/1594)
15-29.9 (Stage 4)	12.7 (61/1801)	25.2 (81/1078)	65.9 (257/977)

Brenda et al JAMA 2010;303(5):423-429



Chronic Kidney Disease Hypertension Goals of Therapy

- Lower BP *without decreasing enjoyment of life*
- Prevent cardiovascular disease
- Slow progression of progressive renal failure



Hypertension Guidelines in CKD

- Current US Guidelines:
 - JNC 7 - 2003
 - KDOQI - 2003
- Updated Guidelines from UK:
 - NICE* # 73 CKD 2008
 - NICE* #127 - August 2011

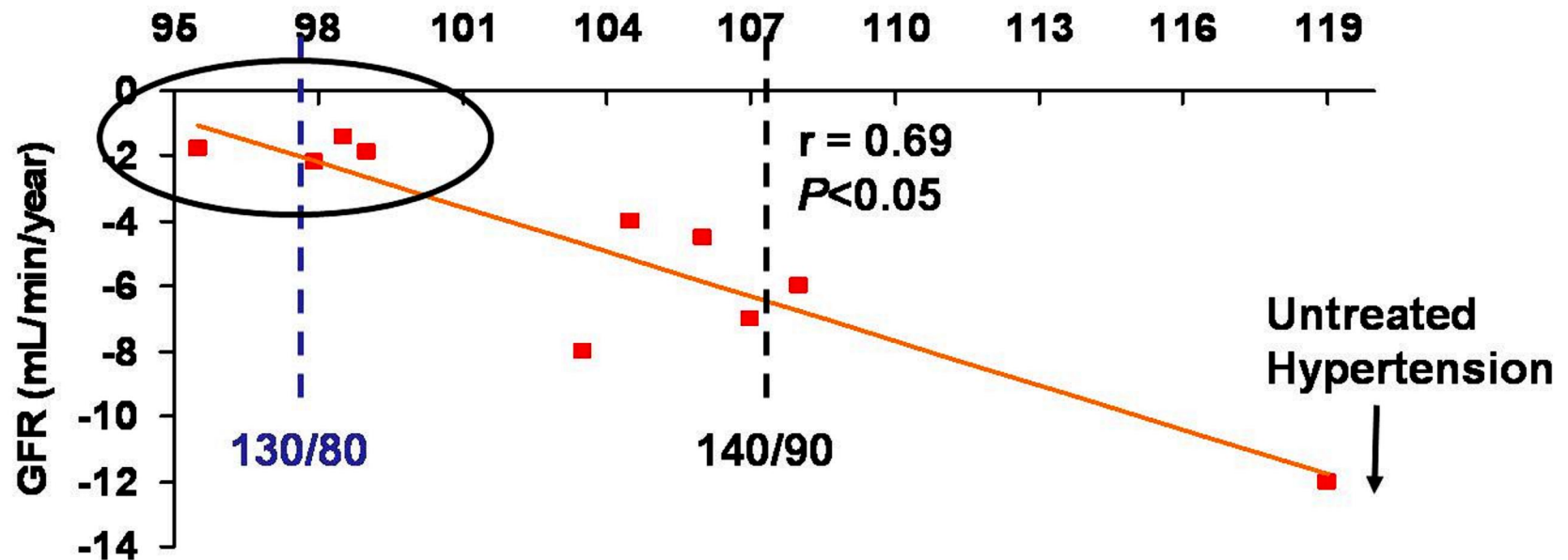
**National Institute for Health and Clinical Excellence*

Recommendations for BP and RAS Management in CKD

Patient Group	Goal BP (mm Hg)	First Line	Adjunctive
+ Diabetes	<130/80	ACEI or ARB	Diuretics then CCB or BB
– Diabetes + Proteinuria	<130/80	ACEI or ARB	Diuretics then CCB or BB
– Diabetes – Proteinuria	<130/80	No specific preference: Diuretics then ACEI, ARB, CCB, or BB	
EXPECT TO NEED 3+ AGENTS TO ACHIEVE GOALS Recommendations largely consistent across JNC 7, ADA, and K/DOQI			

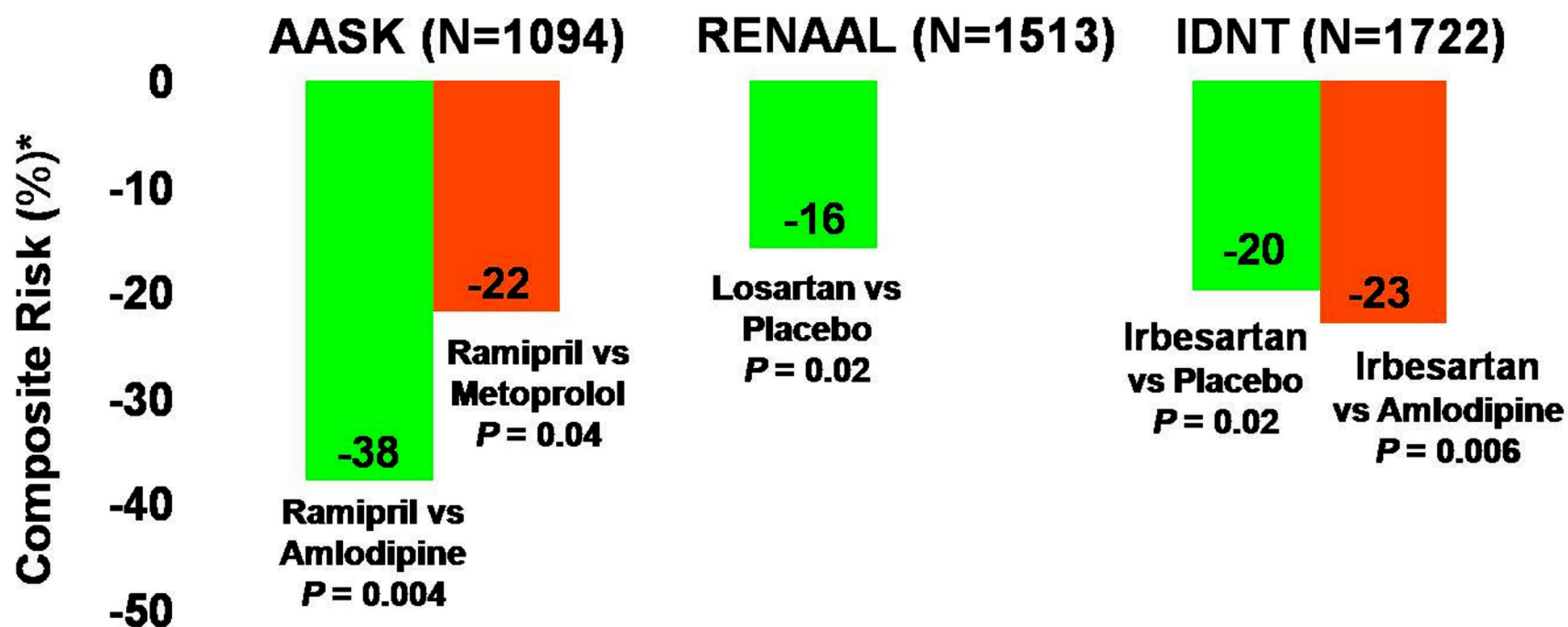
RAS = renin angiotensin system; CCB = calcium channel blocker; BB = β -blocker; JNC 7 = The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. ADA. *Diabetes Care*. 2005;28(suppl 1); Chobanian et al. *JAMA*. 2003;289:2560-2572; Kidney Disease Outcomes Quality Initiatives (K/DOQI). *Am J Kidney Dis*. 2004;43(5 suppl 1):S1-S290.

Relationship Between Achieved BP and GFR



BP = blood pressure; MAP = $[SBP + (2 \times DBP)]/3$ mm Hg. Summary of 9 studies used in figure: Parving et al. 1989; Viberti et al. 1993; Klahr et al. 1993; Hebert et al. 1994; Lebovitz et al. 1994; Moschio et al. 1996; Bakris et al. 1996; Bakris et al. 1997; GISEN Group. 1997. Bakris et al. *Am J Kidney Dis.* 2000;36:646-661.

ACEI/ARB & Reduced Risk of Rapid GFR Decline, Kidney Failure, or Death



Wright et al for the AASK Study Group. *JAMA*. 2002;288:2421-2431. [AASK - African American Study of Kidney Disease and Hypertension].
Brenner

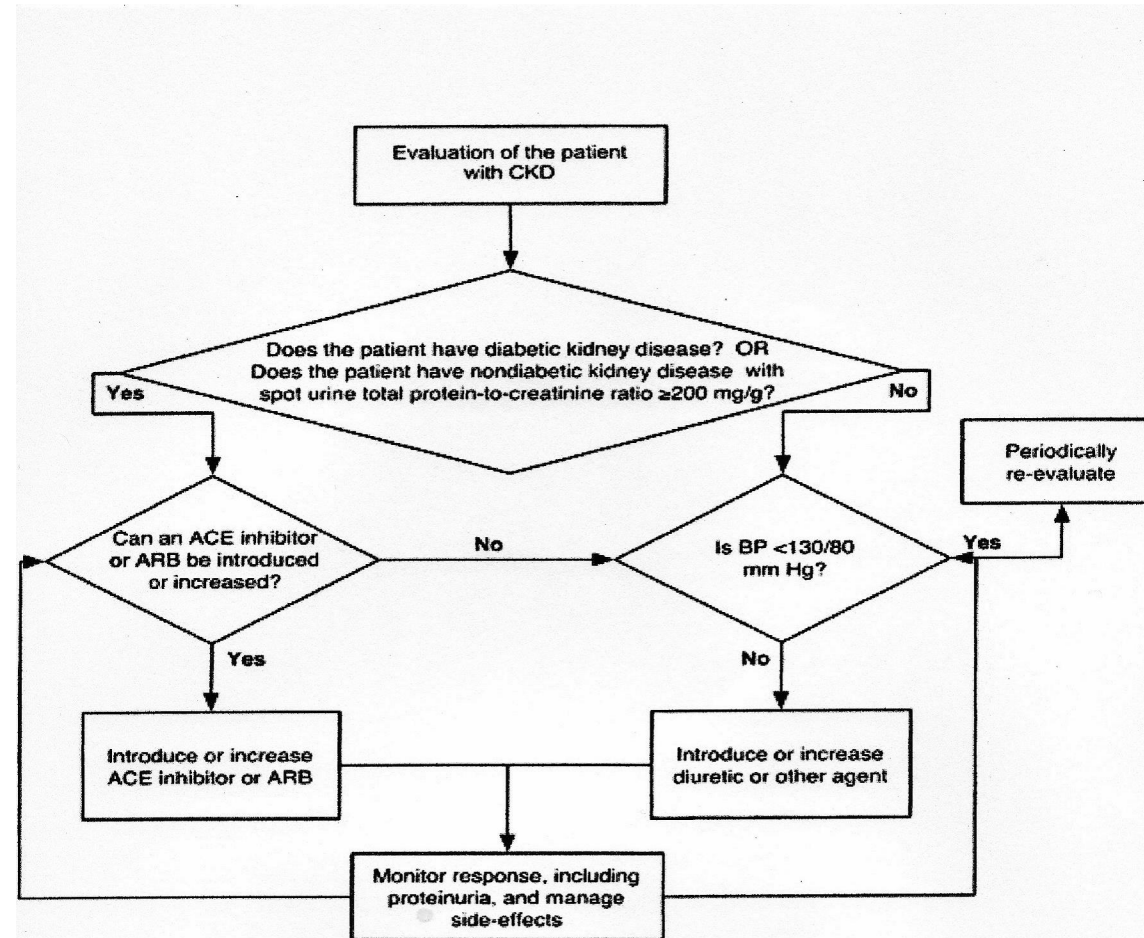
et al for the RENAAL Study Investigators. *N Engl J Med*. 2001;345:861-869. [RENAAL = Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan].
Lewis et al for the Collaborative Study Group. *N Engl J Med*. 2001;345:851-860. [IDNT = Irbesartan in Diabetic Nephropathy Trial.]



K/DOQI Goals of Treatment CKD

- Lower blood pressure
- Reduce risk of CVD in patients *with or without hypertension*
- Slow Progression of KD in in patients *with or without hypertension*
- Take proteinuria into consideration

Algorithm for evaluation on management of hypertension and use of antihypertensive agents in CKD





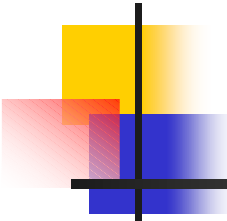
Effects of ACEI and ARBs

- Lower Blood Pressure
- Decrease Intraglomerular Pressure
- Decrease Proteinuria
- Slow Progression of Kidney Disease



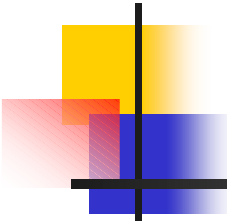
Adverse Effects ACEI/ARBs

- Hypotension
- Worsening of Renal Function
- Hyperkalemia
- Cough
- Angioneurotic Edema
- Rash
- Neutropenia/Agranulocystosis
- Dysgeusia
- Fetal Toxicity



Recommended Intervals to Monitor for Side Effects After **Initiation or Change in Dose** of ACEI/ARB According to Baseline Values

Baseline Value	Systolic BP (mm Hg)	> 120	110-119	< 110
	Baseline GFR (ml/min/1.73 m ²)	> 60	39-59	<30
	Early GFR decline (%)	< 15	15-30	> 30
	Serum Potassium (mEq/l)	≤ 4.5	4.6-5.0	> 5.0
Interval (Weeks)		4-12	2-4	≤ 2



Recommended Intervals to Monitor for Side Effects of ACEI/ARB **When BP at Goal & Dose is Stable** According to Baseline Values

Baseline Value	Systolic BP (mm Hg)	120-129	110-119	< 110
	Baseline GFR (ml/min/1.73 m ²)	≥ 60	39-59	<30
	Early GFR decline (%)	< 15	< 15	< 15
	Serum Potassium (mEq/l)	≤ 4.5	4.6-5.0	> 5.0
Interval (Months)		6-12	3-6	1-3



NICE Guidelines CKD (2008)

Goals

CKD No Diabetes No proteinuria	<140/90
CKD Diabetes	<130/80
CKD Proteinuria 1.0Gms/24 hrs	< 130/80



Stages and Prevalence Chronic Kidney Disease

Stages	eGFR (ml/min/1.73m ²)
Stage 5	< 15
Stage 4	15-29
Stage 3b	30-44
Stage 3a	45-59
Stage 2*	60 -89
Stage 1*	> 90

Use suffix (P)
to denote
presence of
proteinuria

NICE CKD 73
2008

*** With structural or functional abnormalities**



Nice Guideline offer ACEI/ARB

CKD	Diabetes	High BP	Proteinuria
+/-	+	+/-	- 30 mg/24 hrs
+	-	+	- 0.5 Gms/24 hrs
+	-	-	- 1.0 Gms/24 hrs



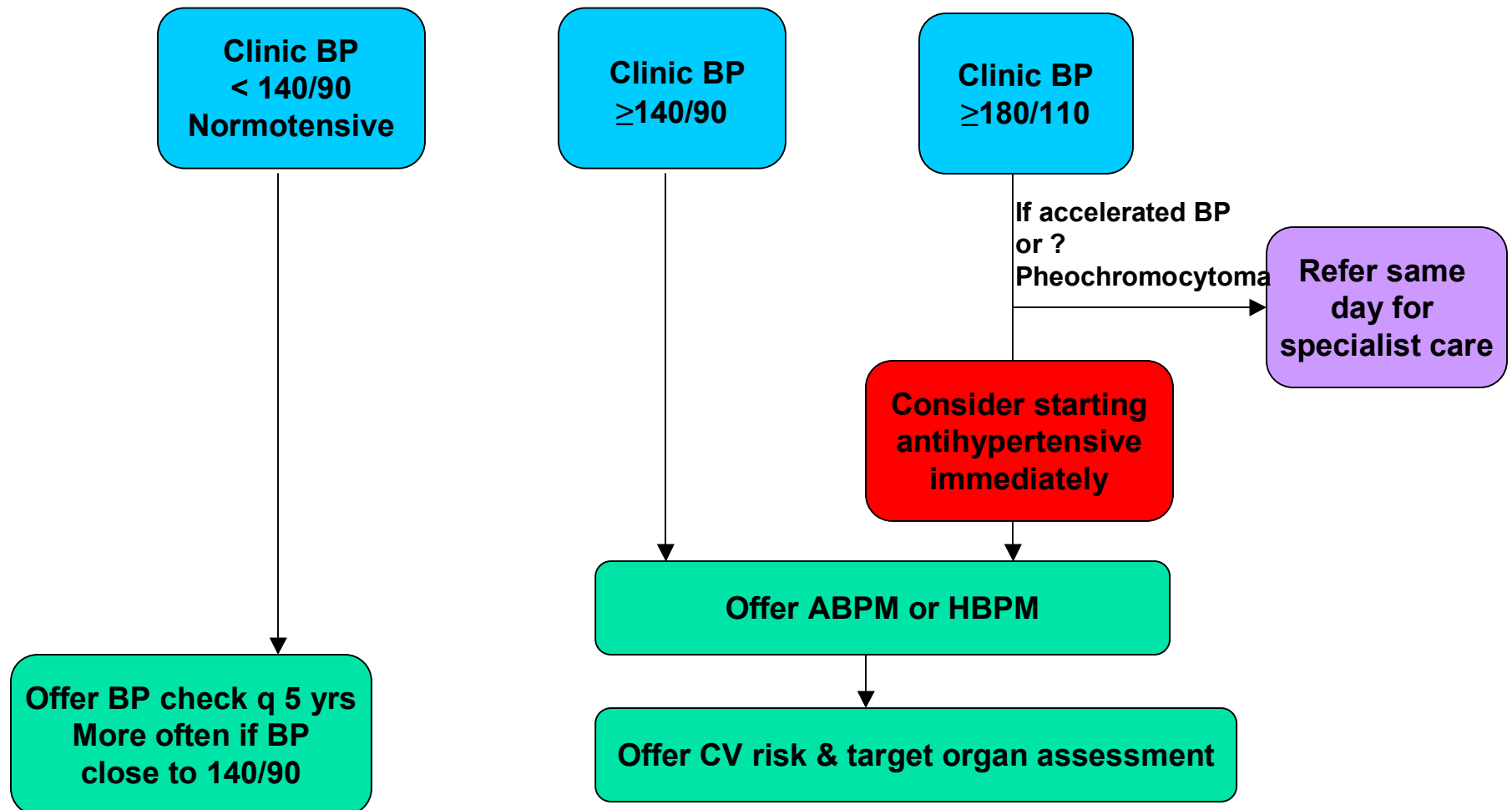
Nice Guideline

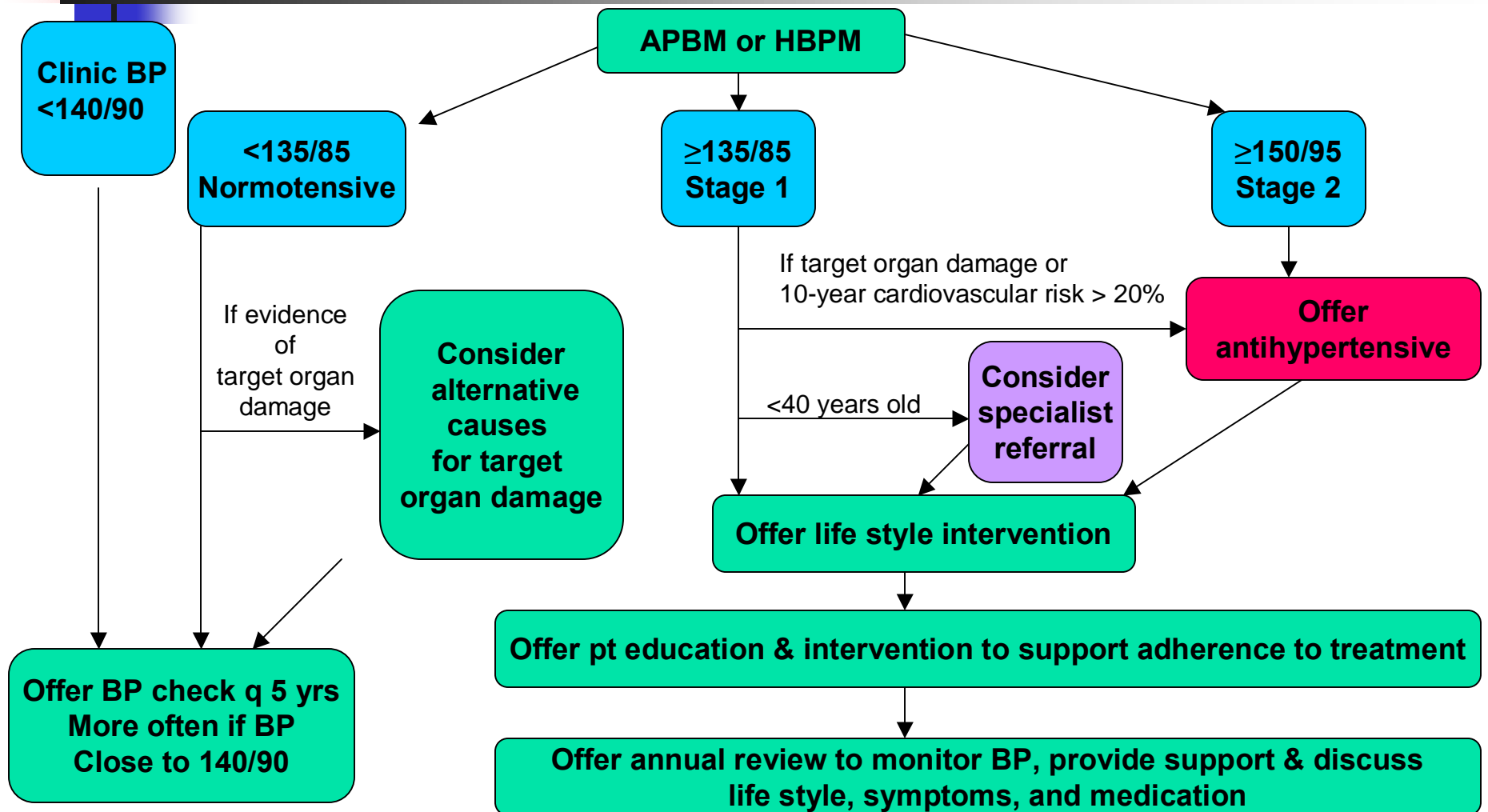
ACEI/ARB

- Start with ACEI switch to ARB if intolerance to ACEI
- When using ACEI/ARB titrate to maximum therapeutic dose before added second agent
- Inform patients about:
 - Achieving optimal tolerated dose
 - Monitoring eGFR and serum potassium

Diagnosis of Hypertension

NICE 2011







Prescription medications (Seniors)

- 41 % Take 5 or more medications
- 54 % have 2 or more physicians
- 36% use 2 or more pharmacies
- 40 % do not take, skip doses, or stop medicine
 - Side effects or feels does not work
 - Cost



Prescription medications

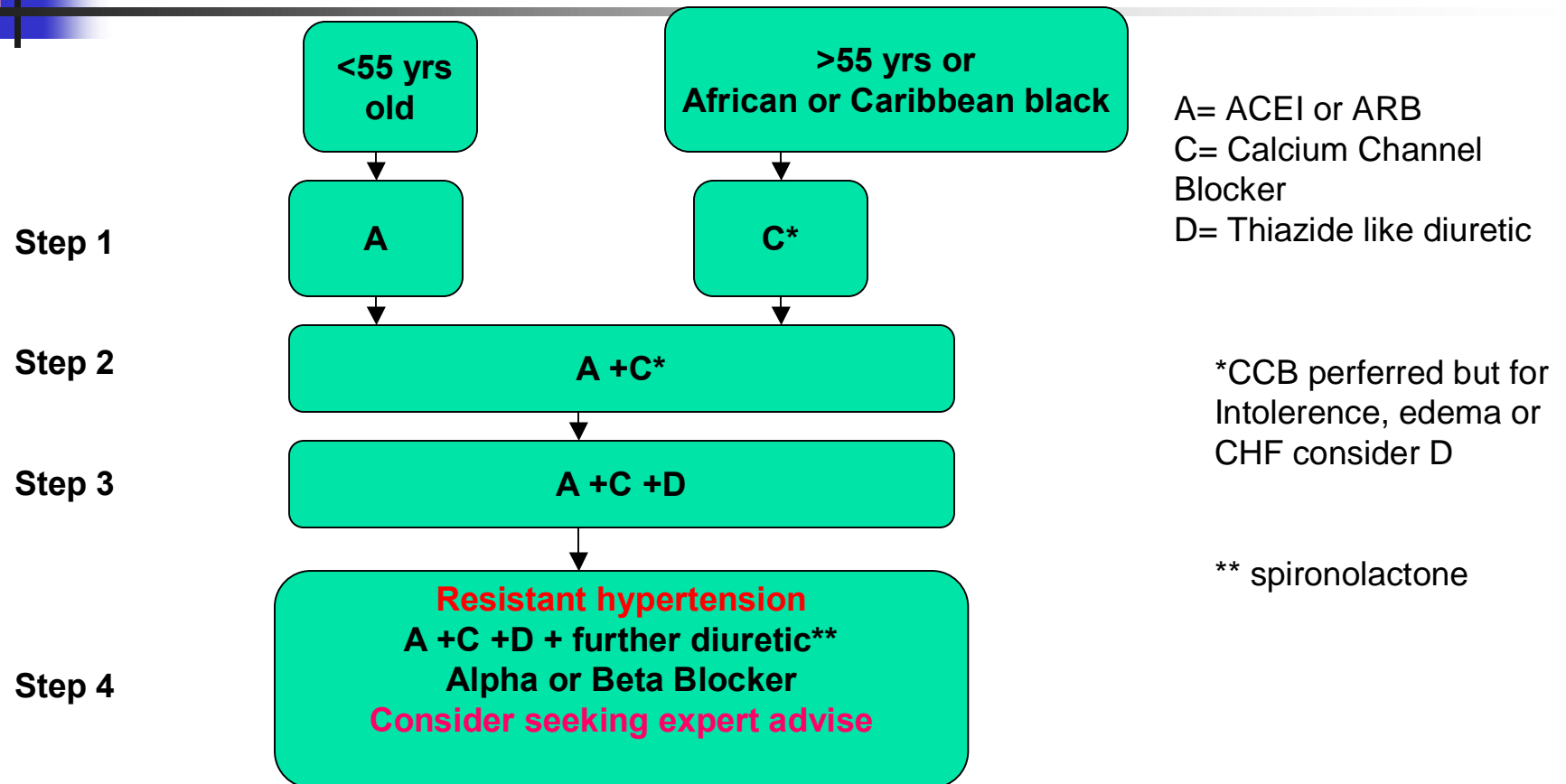
Talk with doctor

Patients who do not take, skip doses, or stop medicine:

- Side effects or feel does not work :
27% do **NOT** talk with their doctor about it
- **Cost:** 39 % do **NOT** talk with their doctor about it.

Hypertension Treatment

NICE





Nice Targets General Population

	Clinic	Home
Below 80 yrs	140/90	135/85
Above 80 yrs	150/90	145/85



Ambulatory/Home BP

- White coat hypertension
 - Drug resistance
 - Hypotensive symptoms with meds
 - Episodic hypertension
 - Autonomic dysfunction
-
- Usual night BP decrease 10-20% (Dipping)
 - Self measured BP $>135/85$

MAPEC

Monitorización Ambulatoria para Predicción de
Eventos Cardiovasculares



Ambulatory Blood Pressure Monitoring for the Predication of Cardiovascular Events

Chronobiology International
27(8): 1629-1651

The logo graphic consists of a vertical black line intersecting a horizontal black line. To the left of the intersection, there are three overlapping squares: a yellow one at the top, a red one in the middle, and a blue one at the bottom. The word "MAPEC" is written in a large, blue, sans-serif font to the right of the graphic.

MAPEC

- 48 hour ABPM initially and annually
- 2056 patients
 - 1084: AM doses only
 - 1072: At least one dose PM
- Median F/U 5.6 years

Results:

- Mean awake BP NS different
- Lower mean sleep-time BP
- Reduced prevalence of nondipping

MAPEC

Event Free Survival Curves

Events:(255)

40 deaths

35 MI

43 Angina

26 Coronary Revascularization

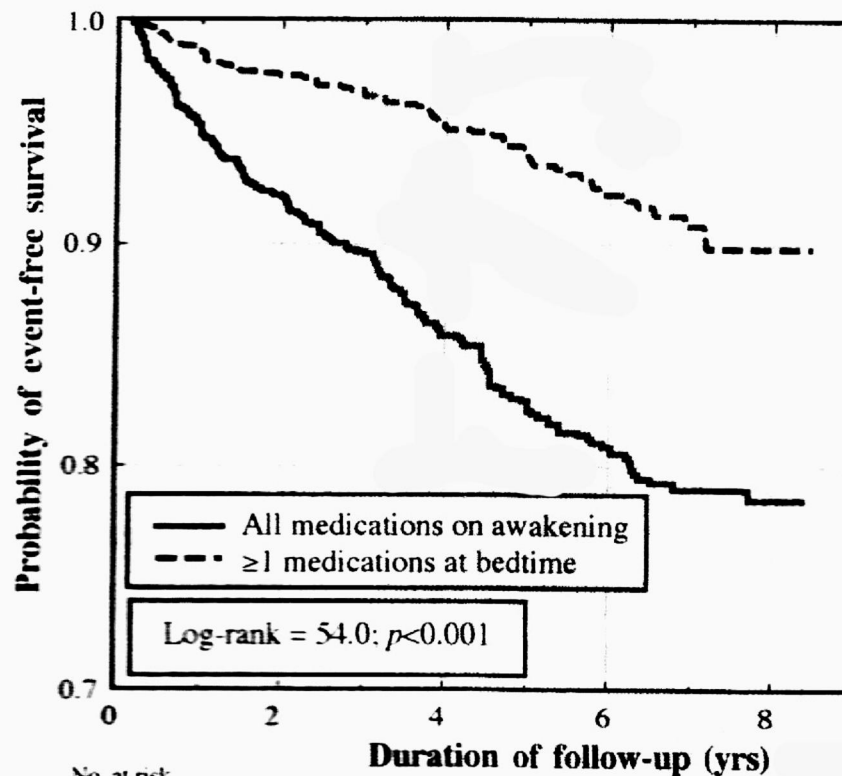
41 Heart Failure

17 Aortoiliac Occlusive Disease

31 Cerebrovascular events

22 Thrombotic Occlusion of

Retinal Artery



No. at risk

Awakening

Bedtime

1084

1072

928

955

676

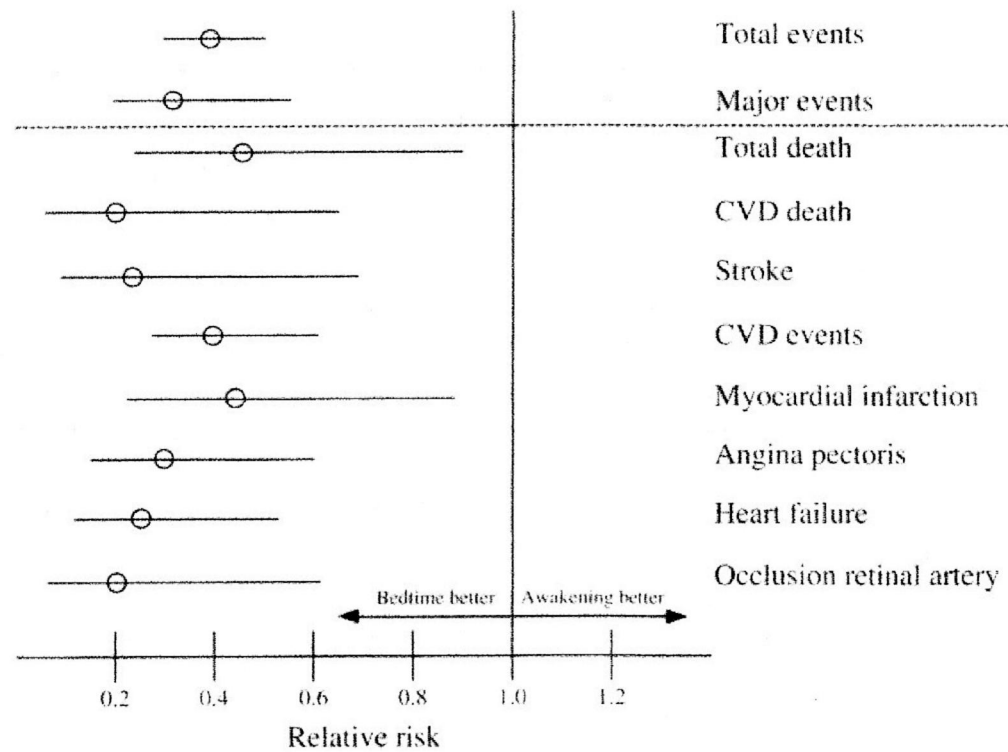
707

478

558

MAPEC 2

RR Total Events=
0.39





Bedtime Antihypertensive Dosing in CKD

- 661 patients with CKD randomized into:
 - All meds AM
 - At least 1 med HS
- 48 hr ABPM and q 3 mo with dose changes or annually
- HS dosing:
- Total Cardiovascular events (HR 0.31)
- Lower sleeptime BP



Summary (1)

- Renal disease and hypertension have a reciprocal relationship
- All hypertensive and all diabetic patients should be screened for CKD
- Control of BP and RAS blockade is essential in treating CKD and Diabetes +/- hypertension
- US guidelines are in need of updating



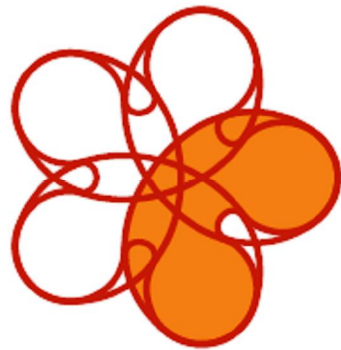
Summary (2)

- We need a fresh look at the use of home and ABPM
- More studies need to be done on PM dosing of BP meds*

*Not evidenced based at this time



Thanks to:



National Kidney
Foundation®



Questions ?